REMARKS

In the final office action, claims 19-53 have been rejected under §103. In response, Applicants have cancelled claim 21, 22, 25 and 26 and amended claims 19, 23, 24 and 27, and provide the herein remarks. Claims 19, 20, 22-24 and 27-53 are pending in the application.

Amendments to Claims

Claim 19 has been amended to add the limitations of cancelled claims 21 and 22 . In particular, claim 19 now recites that endocrine cells are eliminated from the isolated pancreatic cells by means of density gradient centrifugation to obtain exocrine cells in a pellet, prior to inducing dedifferentiation. Thus, only exocrine cells remain. Claims 23, 24 and 27 have been amended to change the dependency of the claims.

The Invention

The present invention provides a method for preparing *in vitro* pancreatic cells capable of secreting insulin. The method utilizes exocrine cells which count for more than 95% of the cells present in pancreatic tissue, rather than using isolated stem cells.

Applicants have surprisingly discovered that inducing dedifferentiation of exocrine cells under the claimed culture conditions produces ductal precursor cells. The ductal precursor cells grown under the claimed culture conditions induce transformation of the cells into insulin secreting endocrine cells.

Response to The Examiner's Remarks in the Office Action

First, Applicants would like to thank Examiner Lankford for taking the time to discuss and review a draft of proposed amended claims faxed on August 12, 2004.

In the office action, the Examiner states that the arguments in the previously filed response were not persuasive and that the claims remain rejected under §103 for the same reasons put forth in the first office action.

The Examiner points out that the claims are not limited to the use of exocrine cells in accordance with the arguments made. In response, Applicants have amended the claims to be limited to the use of exocrine cells. In particular, the exocrine cells of the claimed invention are obtained by using density gradient centrifugation. As a result of the density gradient centrifugation, exocrine cells devoid of endocrine cells are recovered in a pellet.

Rejections Under 35 U.S.C. §103(a)

Claims 1-3 and 6 have been rejected under §103(a) as being unpatentable over Bonner-Weir et al. (PNAS, July 5, 2000; vol. 97, no.14:7999-8004) or Bonner-Weir et al. (WO 00/78929).

According to the Examiner, both Bonner-Weir et al. documents teach the enzymatic isolation of pancreatic cells, the dedifferentiation thereof, and the subsequent dedifferentiation into insulin producing cells.

The Examiner notes that it is not clear if Bonner Weir et al. disclose all of the claimed limitations. However, according to the Examiner, the references clearly indicate that the various proportions and amounts of ingredients used in the claimed method are result effective variables that would be routinely optimized by the skilled practitioner.

The Examiner contends that because "the references clearly set forth which cells are to be isolated from the pancreas, using any known method to do so would have been obvious at the time the invention was made." See page 4 of the office action. Applicants respectfully disagree.

The PNAS 97 document discloses a method for preparing pancreatic cells capable of secreting insulin from pancreatic duct cells. In the document, the preferred cells utilized are not recovered from the pellet after density gradient centrifugation. In fact, PNAS 97 discloses that the pellet of the gradient contains less than 1% islet cells, and that these cells do not secrete insulin when grown in culture. See page 7999, right column, first full paragraph, and page 8002, left column, first paragraph.

The present invention utilizes exocrine cells obtained from the pellet formed as a result of density gradient centrifugation. As mentioned above, PNAS 97 teaches away from using cells obtained from the pellet of the gradient when attempting to culture cells that will secrete insulin.

Accordingly, Applicants respectfully submit that the claimed invention is not unpatentable in view of PNAS 97.

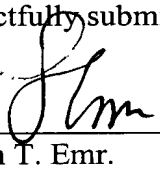
The WO document discloses a method for preparing pancreatic cells capable of secreting insulin from pancreatic duct cells. In the WO document, the cells are separated after being cultured in a flask. The cells that do not attach to the flask are removed. The WO document does not disclose or suggest the separation of cells using density gradient centrifugation.

As discussed above, the present invention utilizes density gradient centrifugation to separate exocrine cells from the cell population. Therefore, because the WO document does not disclose or suggest all of the claim limitations, the present invention can not be unpatentable over the WO document.

Accordingly, Applicants respectfully request that the Examiner reconsider and withdraw the rejection of claims based on PNAS 97 or the WO document.

It is now believed that this application is in condition for allowance. If resolution of any remaining issues is required prior to allowance of the application, and the Examiner believes a telephone discussion with Applicants representative may be helpful, she is cordially invited to contact Applicants' attorney at the telephone number provided below.

Respectfully submitted,



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